REMARKS

Favorable reconsideration is respectfully requested in view of the above amendments and following remarks. Applicants hereby elect Group I, sub-invention (B). The elected invention is encompassed by claims 21-29.

The specification has been amended to address formal issues. Claims 7, 13 and 15-20 have been canceled without prejudice or disclaimer. Claims 21-29 are new. Claim 21 is supported for example by page 6, line 17, page 13 lines 4-9, and page 15, lines 4-9. Claim 22 is supported for example by page 8, lines 6-9, page 8, lines 18-21 and page 9, lines 2-4. Claims 23 and 29 are supported for example by page 15, lines 4-9. Claim 24 is supported for example by page 6, line 17, page 13, lines 10-21 and page 15, lines 10-25. Claim 25 is supported for example by page 8, lines 6-9, page 8, lines 18-21 and page 9, lines 2-4. Claim 26 is supported for example by page 6, line 17, and page 13, line 22 to page 14, line 3. Claim 27 is supported for example by page 6, line 17, page 14, lines 4-9 and page 10, lines 4-6. Claim 28 is supported for example by page 6, line 17, page 14, lines 10-15 and page 16, lines 6-15. No new matter has been added. Claims 21-29 are pending.

Information Disclosure Statement

Applicants respectfully note that US Patent No. 6,194,187, which corresponds to JP 10-000093, was included in the IDS submitted on April 26, 2006. Applicants respectfully submit that a submission of an English-language translation is obviated.

Claim Objections

The claims have been objected to for informalities. The objection is rendered moot, as the previous claims have been canceled. Applicants respectfully submit that the new claims are in proper form and recite the subject matter that was elected.

Claim Rejections – 35 USC §112

Claim 7 is rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully submit that claims 21-29 are definite. Claims 21-29 specifically recite that the ASK1 protein is composed of an amino acid sequence of GenBank Database Registration Number D84476, which is supported by page 6, line 17 of the specification. The functions of the ASK1 protein composed of such a sequence is described

in the GenBank Database under Registration Number D84476 as an apoptosis inducer, and a mammalian MAPKKK that activates SAPK/JNK and p38 signaling pathways. Accordingly, Applicants respectfully submit that claims 21-29 are limited to an ASK1 protein having a specific amino acid sequence and structure, and that the function of the recited ASK1 protein is supported in the specification. In addition, claims 21-29 specifically set forth steps to practice the method of screening a drug for at least one of prevention and treatment of cardiac failure. Therefore, Applicants respectfully submit that claims 21-29 are definite.

Claim 7 is rejected under 35 USC 112, first paragraph, for lack of enablement. The rejection contends that the specification, while being enabling for identifying agents that affect the kinase activity of ASK1 using cells expressing the ASK1 taught by Saitoh et al., does not reasonably provide enablement for identifying agents that affect the kinase activity of any ASK1 having any structure, wherein the ASK1 affects cardiac function. Applicants respectfully submit that claims 21-29 comply with the enablement requirement. Specifically, claims 21-29 recite an ASK1 protein which is composed of an amino acid sequence of GenBank Database Registration Number D84476. Accordingly, claims 21-29 are limited to screening for a drug capable of suppressing apoptosis induced by a specific ASK1 protein that has a known structure with known activities. Applicants respectfully submit that the method for screening a drug that affects the activity of the ASK1 protein as required by claims 21-29 are supported by the specification, and therefore, claims 21-29 comply with the enablement requirement.

Claim 7 is rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully submit that claims 21-29 comply with the written description requirement. Claim 21-29 specifically recite an ASK1 protein that has a specific structure and function. Applicants respectfully submit that the specific amino acid sequence of the recited ASK1 protein and its function are supported by the specification, and therefore, claims 21-29 comply with the written description requirement.

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Claim Rejections – 35 USC §103

Claim 7 is rejected under 35 USC 103(a) as being unpatentable over Hirotani et al., in view of Saitoh et al., as evidenced by Sorescu et al. Applicants respectfully traverse the rejection.

Hirotani teaches that ASK1 is involved in ROS-stimulated cardiomyocyte hypertrophy. However, Hirotani notes that ASK1 activation leads to cell survival, and that their results suggest that ASK1 has a broad range of biological activities depending on cell types and stresses. The reference further notes that cardiac hypertrophy is an adaptive physiological process in response to various extracellular stimuli, such as mechanical stress and cytokines, and that their studies indicate that ASK1 functions as a stress-adaptation signaling intermediate in cardiomyoctes. As such, nothing in the reference suggests that ASK1 is involved in cardiac failure, let alone a method of selecting a medicinal component that inhibits apoptosis induced by ASK1 protein from a drug candidate compound for the prevention and treatment of cardiac failure as required by claims 21-29. In fact, the opposite seems to be suggested by Hirotani. That is, since hypertrophy is a compensation mechanism in response to stress induced by ROS and the like, the reference seems to suggest that the compensation mechanism could be prolonged by maintaining ASK1 protein activity, thereby teaching away from a method of screening for a drug that inhibits ASK1 protein activity as required by the claims. Accordingly, claims 21-29 are patentable over Hirotani.

The rejection relies on Saitoh for assaying ASK1 kinase activity and identifying inhibitors of the activity and Sorescu for motivation to screen for drugs useful in the prevention or treatment of cardiac failure. However, Saitoh and Sorescu do not remedy the deficiencies of Hirotani. The rejection contends that it would have been obvious to a person of ordinary skill in the art to use the methods of Saitoh to identify inhibitors of ASK1 activity in cardiac cells, and that motivation to do so derives from the desire to screen for drugs useful in the prevention or treatment of cardiac failure. The rejection bases this argument on Sorescu's comment that chronic release of ROS has been recently linked to the development of left ventricular hypertrophy and heart failure. However, Sorescu in no way teaches or suggests that a drug inhibiting apoptosis induced by ASK1 protein would be useful in the prevention and treatment of cardiac failure. In fact, Sorescu notes that progression to end-

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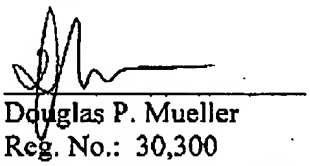
stage heart failure requires certain factors such as cytokines that are initially activated as compensatory mechanisms to stimulate a hypertrophic phenotype in remnant cardiac myocytes and fibroblasts. Given the teachings of Hirotani as described above, the evidence in Soresecu seems to support the notion that it actually might be beneficial to maintain ASK1 protein activity to prolong the compensatory mechanism. To the contrary, as mentioned above, Applicants have unexpectedly found that inhibiting ASK1 protein activity is actually beneficial for the prevention and treatment of cardiac failure. Furthermore, although Saitoh teaches that a constitutively active ASK1 protein can be used, the reference merely uses the constitutively active ASK1 protein as a tool to study the specific effects of Trx on ASK1, and is far from suggesting a method of screening for a drug that is beneficial for the prevention and treatment of cardiac failure, by utilizing as an indicator for selection, the inhibition of apoptosis induced by ASK1 protein. Accordingly, claims 21-29 are patentable over the references taken alone or together.

In view of the above, favorable reconsideration in the form of a notice of allowance is requested. Any questions or concerns regarding this communication can be directed to the attorney-of-record, Douglas P. Mueller, Reg. No. 30,300, at (612) 455.3804.

Respectfully Submitted,

Dated: March 4, 2008



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